Substance Abuse Among Patients with Schizophrenia Spectrum Disorders

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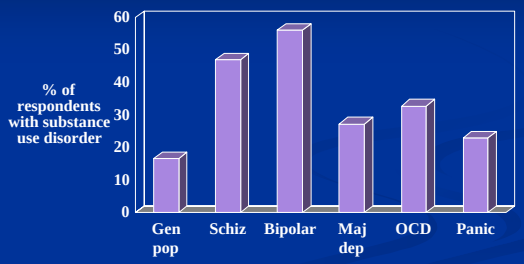
Prevalence of substance use disorders in mental illness



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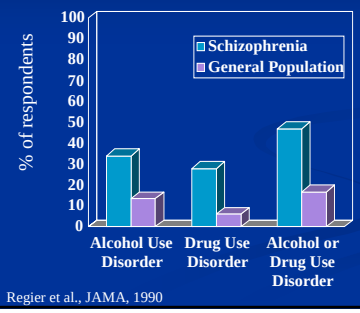
Prevalence of Co-Occurring Disorders-ECA Study



Regier et al., JAMA, 1990

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Dual disorders lead to worse outcomes than single disorders

- Relapse and hospitalization
- Treatment non-adherence
- Violence, victimization, and suicidal behavior
- Homelessness and incarceration
- Medical problems, HIV & Hepatitis risk behaviors and infection
- Family problems
- Increase service use and cost

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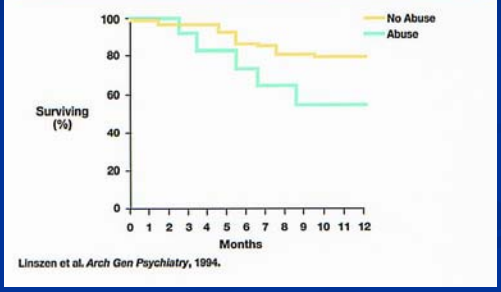
SURVIVAL CURVES OF TIME UNTIL PSYCHOTIC RELAPSE BY NO ABUSE AND ABUSE OF CANNABIS



Linszen et al. *Arch Gen Psychiatry*, 1994.

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Characteristics Associated with Medication Nonadherance

in Six-Month Longitudinal Study

Characteristics	Odds Ratio	95% CI
Substance Abuse	8.1	2.5-26
Observed Side Effects	0.13	0.01-1.2
Outpatient Contacts	0.53	O.25 -1.1

Owen et al, Psychiatric Services 1996

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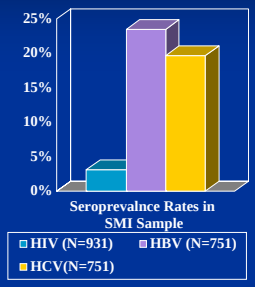
Medical Complications of Co-Occurring Substance Use: HIV and Hepatitis B and C



Persons with Substance Use Disorders had
3 times higher chance of having HIV
2 times higher chance of having HBV
2. 5 times higher chance of having HCV

Rosenberg et al., A Jl Public Health, 2001

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Monthly Income and Expenditures for Substances

Among 105 Patients with Schizophrenia

- Monthly income $650
- Disability income $645
- Expenditures for illegal drugs $250
- Expenditures for alcohol $10
  - Median values

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Costs of treatment for persons with dual disorders

Treated for Substance Use (N=1,493)	Not treated for Substance Use (N=4,394)	No substance use (N=10,509)
$22,917	$20,049	$13,930

Dickey and Azeni, Am J Public Health, 1996

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Why do Schizophrenia and Bipolar Disorder Have the Highest Prevalence of Co-Occurring Substance Abuse?

- Stress-vulnerability model
- Self-medication hypothesis
- Reward deficiency syndrome

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Stress-Vulnerability Model

- Onset/relapse of disorders precipitated by
  - Genetic, early environmental vulnerability
  - Environmental stressors
- Cannabis associated with earlier onset (COMT)
- SCZ pts highly sensitive to substances
  - Relapse
- Vulnerability to SCZ and SUD related?
  - Familial studies fail to find increased SA in families with SCZ, and v.v.

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Self-Medication Hypothesis

- Substance use may decrease negative symptoms, EPS
- Psychotic symptom responses variable
- Non-specific escape

- Comorbid pts have fewer negative sxs
- First-episode SCZ patients have similar rates of SUD before exposure to meds

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Reward Deficiency Syndrome

- Mesocorticolimbic DA circuit mediates schizophrenia and brain reward system
- Reward system mediates pleasure, contentment & motivation
- Substances of abuse exert reinforcing effects via brain reward system
- Reward deficiency creates vulnerability to addiction

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An Animal Model Test of the Reward Deficiency Hypothesis

- Neonatal hippocampal lesions in rats (animal model for schizophrenia)
- Disrupts reward circuit to prefrontal areas
- Lesioned rats demonstrated increased self-administration of cocaine relative to controls

Chambers, 2001

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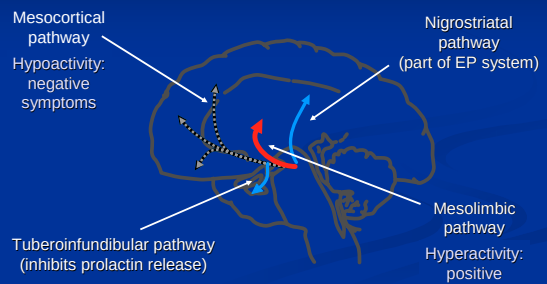
Dopamine Hypothesis of Schizophrenia



Adapted from Inoue and Nakata. *Jpn J Pharmacol.* 2001;86:376.

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Mesocorticolimbic Circuit

- Mesolimbic: VTA → nucleus accumbens
- Mesocortical: VTA → PFC → mesolimbic
- Slow, irregular basal firing & burst firing
- PCP animal models of schizophrenia
  - ↑ rate & regularization of basal firing
  - ↑ burst firing in mesolimbic tracts
  - ↓ burst firing in mesocortical tracts

Svenson, 1995

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Pharmacologic Effects on Reward Circuitry

- 5HT2 antagonism + weak D2 antagonism: ↑ burst firing in hypoactive mesocortical DA neurons (facilitating reward)
- α-1 + D2 antagonism: ↓ burst firing in overactive mesolimbic DA neurons
- α-2 antagonism: deregularization of basal firing (↑ signal detection)

Svenson, 1995

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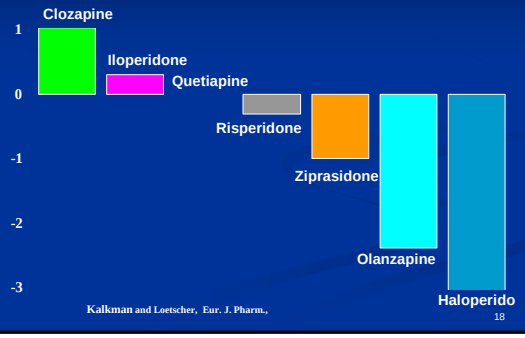
Comparison of α_{2C}/D_2 ratios



Kalkman and Loetscher, Eur. J. Pharm.,

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Impact of Clozapine on SA

- Case reports: ↓ alcohol, drug & cigarette use, ↓ cocaine craving (ie: Albanese 1994)
- Drake 2000: N=151 naturalistic, prospective CLZ 67-79% remission vs CON 34%
- Zimmet 2000: N=58 retrospective CLZ 85-93% reduction, 72-80% abstinence, 0% relapse

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Impact of Risperidone on SA

- Newton 2001: N=9, 10-20% reduction in high & stimulation following IV cocaine
- Smelson 2002: 18 detoxed inpts, RSP ↓ craving (movie) and relapse vs CON
- Green 2003: N=32, retrospective CLZ 54% abstinence vs RSP 12%

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Impact of Olanzapine on SA

- Tsuang 2002: N=4, RCT; OLZ ↓ cocaine craving and use vs HAL no change
- Longo 2002: 2 cocaine addicts, OLZ ↓ cocaine craving and relapse
- Littrell 2001: N=30, 70% full remission (100% cocaine), ↓ dysphoria, ↑ hope
- Noordsy 2001: N=105, OLZ - significant pre-post ↓ substance abuse, n.s. vs CON

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Impact of Quetiapine on SA

- Brown 2001: N=29 randomized CON d/c
  - 8 psychotic relapse → QTP
  - ↓ cocaine craving in d/c & QTP vs. CON
- Brown 2001: N=17 psychotic: QTP add-on
  - ↓ cocaine craving, psychiatric sxs
  - Change in drug use: n.s.
- Longoria 2003: N=14
  - ↓ alcohol craving and days of use

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Nicotine Dependence

- Bupropion effective among people with schizophrenia (George 2000, Evins 2001, Weiner 2001)
- George 2002: N=32, RCT, novel APs significantly enhanced effect of bupropion
  - Abstinence rates: CON 0/10 = 0%
  - RSP 2/6 33%, CLZ 1/1 100% OLZ 5/5 100%

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Ziprasidone & Aripiprazole

- Klotz 2003: N=69 (40 PD/29 SUD) naturalistic ziprasidone IM for agitation
  - Similar efficacy and tolerability
  - no analysis of co-occurring, nor SA outcomes
- Aripiprazole: No studies to date

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How do people obtain remission from dual disorders?

- Stable housing
- Sober support network/family
- Regular meaningful activity
- Trusting clinical relationship
  - Alverson et al, Community MHJ, 2000

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Integrated Dual Disorders Treatment

- More effective than separate treatment
- 20 studies show integrated treatment is more effective than traditional separate treatment
  - (Drake et al, Schiz Bull 1998 and Drake et al, Psych Services 2001 for summaries).

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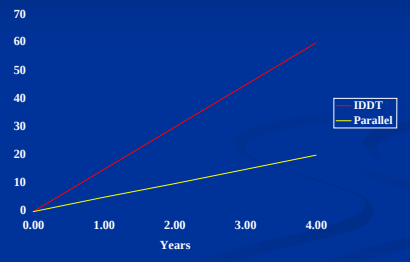
IDDT Improves Abstinence Outcomes



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Principles of Integrated Dual Disorder Treatment

- Integration of mental health and substance abuse treatment
  - Same team of dually trained people
  - Same location of services
  - Both disorders treated at the same time
- Stage-wise treatment
  - Different services are effective at different stages of treatment

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Stagewise Treatment

- Precontemplation - Engagement
  - Outreach, practical help, crisis intervention, develop alliance, assessment
- Contemplation & Preparation - Persuasion
  - Education, set goals, build awareness of problem, family support, peer support,
- Action - Active Treatment
  - Substance abuse counseling, medications, skills training, family, self help, groups
- Maintenance - Relapse prevention
  - Relapse prevention plan, skills training, expand recovery to other areas of life

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Integrated Dual Disorders Treatment

- Assertive outreach
- Motivational substance abuse counseling
- Dual disorder groups
- Training for rehabilitation of skills
- Social and family support interventions
- Long term perspective
- Cultural Sensitivity and competence

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Prescribing Psychotropic Medications for Patients With Dual Disorders

- General guidelines
- Potential risks and interactions

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General Guidelines

- Determine mental illness and substance abuse diagnosis
  - Avoid treating substance induced symptoms
  - Do not withhold meds due to substance use
- Treat both disorders as primary
  - No empirical support for primary-secondary distinctions

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General Guidelines

- Use meds with low abuse potential
- Use meds with low lethality
- Consider psychotropic meds with potential to ↓ craving or substance use
- Consider anti-addiction meds
- Dispense limited amounts
- Close monitoring

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Medication-Drug Interactions

- Conventional antipsychotics
  - possible increased risk of dystonia, akathisia, and tardive dyskinesia
  - risk for hyperpyrexia in combination with stimulants
  - cigarette smoking lowers blood levels
  - lower seizure threshold (as do cocaine use & sedative withdrawal)

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Medication-Drug Interactions

- Novel antipsychotics
  - risk of respiratory suppression with combination of clozapine and benzos
  - alcohol may increase sedative effects of clozapine
  - lower seizure threshold (esp clozapine)
  - cigarette smoking lowers blood levels

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Medication-Drug Interactions

- Tricyclic antidepressants
  - chronic alcohol use may induce metabolism and decrease levels
  - additive cardiotoxicity with cocaine

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Medication-Drug Interactions

- MAO Inhibitors
  - tyramine present in alcoholic beverages may produce elevated blood pressure – hypertensive crisis
  - potentiation of sympathomimetic effects of stimulants – hypertension/hyperpyrexia
  - toxic interaction with meperidine (hypertensive crisis)

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Medication-Drug Interactions

- SSRIs
  - possibly lower seizure threshold
- Other antidepressants
  - alcohol or benzodiazepines increase cognitive and motor side effects of mirtazapine
  - venlafaxine elevates blood pressure, as does alcohol use and withdrawal
  - bupropion lowers seizure threshold

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Benzodiazepines in Dual Dx

- 202 pts in integrated Dual Dx ACT
- Interview, chart review, Medicaid records
- Benzo Rx ↑ risk of benzo abuse, but not associated with changes in use of other substances

Brunette, Drake, Noordsy; Psych Services, 2003

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